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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,815	04/30/2001	Gary E. Rehm	MSE #2610	3326

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Jerome L. Jeffers, Esq.
Bayer Corporation
P.O. Box 40
Elkhart, IN 46515-0040

EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/09/2002 5

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,815	REHM ET AL.	
	Examin r	Art Unit	
	Gary W. Counts	1641	

-- Th MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 4 is acknowledged. The traversal is on the ground(s) that the inventions are not unrelated inventions and are not separate and distinct inventions.. This is not found persuasive because restriction requirements are set forth for reasons of patentable distinction between each independent invention so as to warrant separate classification and search. The record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. The requirement is still deemed proper and is therefore made **FINAL** for reasons of record.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4, and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al (US Patent 5,856,117) in view of Berry et al (US Patent 5,384,247).

Uenoyama et al disclose a method for measuring the concentration of urinary trypsin inhibitors which involves mixing an urine sample, trypsin, and a buffer solution and the addition of a substrate solution to cause the enzyme reaction, and measuring the activity of trypsin (col 5, lines 39-60). Uenoyama et al also teach the use of dimethylfomamide as the solvent (col 6, line 11) and a buffered pH of 7.8 (col 7, line 46) and the substrate present in a concentration of 1 to 50 mmol/l (col 4, line 16) and trypsin in the concentration of 10 to 500 mg/l preferably 20 to 100 mg/l (col 5, line 52).

The method of Uenoyama et al differs from the instant invention in failing to disclose the use of a polycarboxylic chelating agent to inhibit interference of calcium present in the urine.

Berry et al (US Patent 5,384,247) teach the use of EGTA and EDTA as chelating agents which inhibit the interfering ions of calcium in a urine sample (col 5, lines 19-39, col 6, line 14-17). The use of these chelating agents reduce the free concentration of interfering ions to levels where interference is no longer significant and increase the sensitivity of the enzyme to an analyte with respect to the interfering ion (col 3, lines 45-52).

It would have been obvious to one of ordinary skill in the art to incorporate the polycarboxylic chelating agents of Berry et al into the method of Uenoyama et al

because Berry et al shows that the use of these chelating agents provide the advantage of reducing the free concentration of interfering ions to levels where interference is no longer significant and also increase the sensitivity of the enzyme to an analyte.

With respect to the specific concentration of the chelating agents recited in the instant claims, the optimum concentration of chelating agent can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art.

3. Claims 5 and 6 rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al in view of Berry et al as applied to claims 1-4 and 7-9 above, and further in view of May et al (GB 2,204,398 A).

See above for teachings of Uenoyama et al and Berry et al.

Uenoyama et al differ from the instant invention failing to disclose dry test reagents and a dry test device which the urine test sample can flow by dipping the dry test device into the buffered assay medium.

May et al disclose a device comprising a hollow casing constructed of moisture-impervious solid material containing a dry porous carrier which communicates indirectly with the exterior of the casing, a sample receiving member protrudes from the casing such that a liquid test sample can be applied to the receiving member and permeate to the porous carrier which contains impregnated reagents (page 15, lines 16-35 and page 16, lines 1-9). This diagnostic test device allows for quick and convenient use and requires the user to perform as few actions as possible (page 2, lines 29-35).

It would have been obvious to one of ordinary skill in the art to use the device of

May et al to practice the method of Uenoyama et al as modified by Berry et al, because May et al shows that the device allows for quick and convenient use and requires the user to perform as few actions as possible, where all the necessary reagents are all present on a single solid support.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ueoyama et al in view of Berry et as applied to claims 1-4 and 7-9 above, and further in view of Nanbu et al (US Patent 6,130,055).

See above fro teachings of Uenoyama et al and Berry et al.

Uenoyama et al differ from the instant invention in failing to disclose arginine or lysine derivatives as the substrate for trypsin.

Nanbu et al discloses a method for measuring the concentration or activity of urinary trypsin inhibitor. Nanbu et al teach mixing a sample, trypsin solution, and a substrate in a solution and measuring the tryspin activity. Nanbu et al also teach that this substrate may come from the amino acid residues of the L-type (col 2, lines 13-23). The use of this substrate would allow for excellent solubility.

It would have been obvious to one of ordinary skill in the art to incorporate the trypsin substrates of Nanbu et al into the method of Uenoyama et al as modified by Berry et al because Nanbu et al shows that the use of the L-type amino acid residues allows for excellent solubility (col 2, line 23).

Response to arguments

Applicants arguments filed January 31, 2002 have been fully considered but they are not found persuasive.

Applicant argues that the teachings of Uenoyama et al. involves the addition of a buffer which contains at least 0.15 umol of calcium per ug of added trypsin. Applicant states that the excess calcium is to reduce the interference of calcium salts already in the urine sample by adding additional calcium to swamp out its effect. It is noted that Uenoyama et al does teach the addition of calcium to the solution. However, the comprising language as recited in the claims would include the inclusion of other components. Unless there is a recitation in the claims which excludes other components, the claim as recited encompasses the teachings of Uenoyama et al. Applicant also argues that in the method used by Uenoyama et al calcium interference is not removed but only offset. It is noted that the calcium is not removed. However, the instant claims as recited do not recite that calcium is removed. Therefore, it is the Examiner's position that the claims still read on Uenoyama's reference because the claims as recited have not excluded the inclusion of other components or the removal of calcium.

Applicant also argues that the method of Berry et al is specific for sodium. It is noted that Berry et al primarily teaches for sodium. However Berry, et al also teaches the method may also be used for calcium (divalent cation). Applicant argues that there is no mention of a selective binding agent which selectively binds to an interferant. As noted in paper number 2, Berry et al does teach the binding of interfering substances. Applicant argues that the effect of ions which are chelated in Berry et al is specific to transferase, hydrolase, oxidoreductase and lyase whereas trypsin is a protease. The Examiner agrees that trypsin is a protease. However, trypsin's are hydrolase enzymes.

Applicant also argues that there is no suggestion in either reference (Uenoyama et al and Berry et al) that chelating agents could or should be used in assays for trypsin inhibitors in which trypsin is the enzyme. It is the Examiner's position that since Uenoyama et al teaches the offset of the effects of calcium, it would have been obvious to one of ordinary skill in the art to attempt alternative methods to offset the effects of calcium in assays for trypsin inhibitors in which trypsin is the enzyme. Further, it is well know in the art to use EDTA or EGTA as a chelating agent to decrease the effects of calcium.

Applicant also argues that Uenoyama et al. and Berry et al. do not render obvious the trypsin inhibitor assay of the present invention in the wet form and the inclusion of May et al. does not render it obvious in the dry form. As noted above it is the Examiners position that Uenoyama et al. and Berry et al. do render obvious the trypsin inhibitor assay of the present invention in the wet form. As stated by Applicant May et al. is cited for its teaching of a dry test device into which the reagents are incorporated into a test strip. Therefore, as noted in paper number 2, it would have been obvious to one of ordinary skill in the art to impregnate reagents in a dry form into a test device.

Applicant also argues that while the substrate for trypsin may be disclosed by Nanbu et al., Claim 10 depends on claim 1 which has been shown to be novel and unobvious. It is the Examiner's position that claim 1 has not been shown to be novel and unobvious. Therefore, as stated by Applicant the substrate for trypsin is disclosed by Nanbu et al and would have been obvious to one of ordinary skill in the art to

incorporate the trypsin substrates of Nanbu et al into the method of Uenoyama et al as modified by Berry et al.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
April 4, 2002

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
04/05/02